Assessment of a silage feed additive consisting of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) NCIMB 30084 for all animal species for the renewal of its authorisation (Chr. Hansen A/S)

Reference Number RP1528

Risk Assessment Unit
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Regulated Product Dossier Assessment
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Contents

Abbreviations

AMR	Antimicrobial resistance
ANI	Average nucleotide identity
CAS	Chemical Abstracts Service
CFU	Colony forming units
EC	European Commission
EU	European Union
EFSA	European Food Safety Authority
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
FSA	Food Standards Agency
FSS	Food Standards Scotland
GB	Great Britain
MIC	Minimum inhibitory concentration
OECD	Organisation for Economic Co-operation and Development
QPS	Qualified Presumption of Safety
RP	Regulated Product
UK	United Kingdom
WGS	Whole genome sequence

1. Executive summary

The FSA/FSS Food Standards Agency and Food Standards Scotland (FSA/FSS) have reviewed an assessment of application RP1528 for the renewal of authorisation of *Lactiplantibacillus plantarum* (previously *lactobacillus*) NCIMB 30084 for its use as a technological additive, functional group of silage additive, in all animal species.

This feed additive application has been made to renew the authorisation in Great Britain (GB) as it is 10 years since the product was authorised and placed on the market in the EU. The same product and uses have been authorised in multiple other countries as the information and data demonstrate the regulatory criteria are met. This feed additive had its application for renewal of authorisation assessed by the European Food Safety Authority (EFSA), which was published in 2023. FSA/FSS have reviewed the information available, including the EFSA renewal opinion[1] and confirmed that *Lactiplantibacillus plantarum* NCIMB 30084, as described in this application, is unlikely to have any adverse effects on human or animal health or the environment in the context of its intended uses in GB.

2. Background and purpose of review

In accordance with Assimilated EU Regulation 1831/2003[2] on feed additives, the application RP1528 for the use of *Lactiplantibacillus plantarum* NCIMB 30084 as a feed additive for all animal species has been submitted for authorisation in each nation of Great Britain (GB).

Whilst it was a Member State of the EU, the UK accepted the risk assessments of the European Food Safety Authority (EFSA) in respect of authorisations for regulated food and feed products. When GB left the EU, it retained the same regulations for food and feed regulated products; FSA and FSS also adopted equivalent technical guidance and quality assurance processes to be able to undertake GB risk assessments for regulated product applications.

To ensure our regulatory systems are risk proportionate and resources are used effectively, FSA/FSS have used the evidence submitted by the applicant and other information in the public domain, including the EFSA risk assessment opinion, to provide a summary assessment of the evidence of safety presented in this report.

Specifically, in reviewing the risk assessment that EFSA have recently completed, the reviewers have verified that the standard approach taken, when compared to the relevant guidance applied in GB, has been followed and the conclusions made are consistent with the data summarised in the opinion. Consideration has been given to the processes undertaken to ensure the EFSA opinion is robust and whether there are any aspects that would require further review, such as specific issues for the countries of GB. The result of the assessment is that there is sufficient evidence of safety to conclude without requiring further risk assessment at this time.

2.1 Applicant

Name:	Chr. Hansen A/S
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2.2 Genetic modification step

Not applicable.

3. Details of other Regulators opinions

The additive *Lactiplantibacillus plantarum* has previously been authorised in the EU by Commission implementing regulation (EU) 308/2013.[3] In Australia silage additives are exempt from registration under Schedule 3 of the Agvet Code Regulations. In 2023, EFSA published a risk assessment opinion[1] on the renewal of application of *Lactiplantibacillus plantarum* NCIMB 30084 for its use as a feed additive. This opinion has been reviewed by FSA/FSS risk assessors.

3.1 Methodology applied in the EFSA opinion

The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) assessed the safety and the efficacy of Lactiplantibacillus plantarum NCIMB 30083 in accordance with Guidance on the renewal of the authorisation of feed additives[4] and principles in Regulation (EC) No 429/2008[5].

3.2 Compound

The current authorization for the additive requires a minimum content of the active agent (*Lactiplantibacillus plantarum* NCIMB 30084) at 5.0×10^{10} colony forming units (CFU)/g of the additive. An average of 4.69×10^{11} CFU/g additive was shown in analysis of 4 fermentation batches (9 samples in total) of additive. It was stated by the applicant that the manufacturing process and the composition remains unchanged since the previous authorization.

The active agent is produced by fermentation. It was originally isolated from silage. The final product includes a maximum of 6% fermentation medium, up to 3% water, 17-42% cryoprotectants, 8% synthetic amorphous silica as an anticaking agent and 50-75% of maltodextrin as a carrier.

3.3 Specification

No new physicochemical or stability data were presented for the additive, as the EFSA Panel stipulated that since the manufacturing process had not changed, the data provided in the previous EFSA opinion (2013)[6] would still apply. Information provided on the identity, composition and specifications of the production species does not raise safety concerns.

Five samples from three batches of the additive were tested for impurities, aflatoxin B1, mercury (Hg), lead (Pb), cadmium (Cd) and arsenic (As) concentrations, Table 1 shows the mean and range values for these concentrations. The EFSA panel concluded that the impurity results did not cause concern.

Table 1: Average and range values for impurities detected in 5 samples of *Lactiplantibacillus plantarum* NCIMB 30084

	Mercury [mg/kg]	**Lead [mg/kg]**	**Cadmium [mg/kg]**	**Arsenic [mg/kg]**	**Aflatoxin B1 [µg/kg]**
Average value	0.006	<0.01	0.014	0.031	<0.46
Value range	0.003-0.014	<0.01	0.01-0.015	0.014-0.047	<0.46

Analysis of 9 samples from 4 batches of the additive demonstrated compliance with predefined specifications: *Escherichia coli* (<10 CFU/g), *Salmonella spp.* (not detectable in 25 g frozen product or 5g freeze dried bulk), yeasts and filamentous fungi (<1000 CFU/g) and coliforms (<1000 CFU/g). A modification to specification for *Salmonella spp.* was made by the applicant in which 5 g instead of 25 g were analysed for 4 batches. In addition, 3 batches were tested for *Enterobacteriaceae* with resulting concentration below the limit of quantification (< 10 CFU/g).

The conclusions of the previous EFSA opinion (2013)[6] stated that stability of three batches were tested in sealed aluminium foil bags at -18, 5 and 25 °C for up to 12 months, and essentially no losses were observed under the conditions tested. Stability in water was also tested using 3 replicates and the viability of the strains was not essentially affected by storage.

3.4 Characterization of the active agent

The average nucleotide identity (ANI) for taxonomical identification was 99.9% with the type strain *Lactiplantibacillus plantarum DSM 20174*^{T}. The strain has undergone no genetic modifications. It was originally isolated from silage.

The broth microdilution method was used to assess the strain's susceptibility to antimicrobials. The strain is considered susceptible to all relevant antibiotics because all the minimum inhibitory concentration (MIC) values were below the specified cut-off values stated in the EFSA FEEDAP Guidance[7]. Kanamycin exceeded the cut-off value by one dilution, which was considered within the normal range of variation by the Panel.

The strain's whole genome sequence (WGS) was examined for the presence of antimicrobial resistance (AMR) genes by cross-referencing against 2 databases. No concerns were identified from the search at nucleotide level with set thresholds for ResFinder, and NCBI Bacterial Antimicrobial Resistance Reference Gene database.

The additive is presently authorised for all animal species, without a specified maximum content, for its use in feed. No changes to these conditions of use were proposed.

3.5 Toxicological data

Lactiplantibacillus plantarum NCIMB 30084 is currently authorised as a silage additive for all animal species as a technological additive.

The opinion under review refers to previous conclusions from the prior 2013 EFSA evaluation[6] to derive conclusions on the safety for the target species, consumers and the environment, following the Qualified Presumption of Safety (QPS) approach to safety assessment, raising no safety concerns for any of these categories.

A literature review presented by the applicant was evaluated. Methodological limitations to the literature review meant it was not considered for the assessment. EFSA confirmed that in 2013, they previously concluded that the use of this strain in the production of silage was considered safe for the target species, consumers and the environment. In the current application, the identity of the strain *Lactiplantibacillus plantarum* NCIMB 30084 was confirmed, and evidence was provided that the strain does not show antimicrobial resistance for antibiotics of human and veterinary importance.[8] Due to this, the EFSA Panel accepts that the conclusions which have been previously reached are still valid.

For safety for the user, no specific data was submitted regarding effects on the skin or eyes and therefore the EFSA Panel could not conclude on skin or eye irritancy of the product. The EFSA Panel concluded that due to the proteinaceous nature of the active agent, the additive should be considered a respiratory sensitiser. It is recommended to use gloves and breathing protection during handling.

3.6 Analytical Method Review

FSA/FSS accept the EURL analytical method evaluation report[9]. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Other regulators opinions and conclusions

EFSA (2023) found that this product, silage additive *Lactiplantibacillus plantarum* NCIMB 30084, raises no safety concerns for the target species, the consumer and the environment.

The EFSA Panel could not conclude on whether the additive is not a skin or eye irritant. Due to the proteinaceous nature of the product, it was considered to be a respiratory sensitiser.

The Panel considered that microbial contamination and chemical impurities do not raise safety concerns.

5. Caveats and uncertainties

No conclusion can be drawn on the skin or eye irritation potential of the additive.

The average content of the active agent within the additive (4.69×10^{11} CFU/g) was derived from only four independent batches.

6. FSA - FSS conclusion for GB risk analysis

The application has been assessed in line with the applicable guidance and is partially based on considerations of detailed proprietary information available to the Panel, whilst this is only briefly summarised this description is consistent with the conclusions. The conclusions of the EFSA opinion have been reviewed in detail by FSA/FSS and are considered appropriate and consistent within the identified caveats and uncertainties identified in the opinion and would be applicable to GB.

7. Outcome of assessment

FSA/FSS has reviewed the applicant's renewal application, supporting documentation, and other regulators risk assessments, most notably the EFSA risk assessment opinion (2023) and consider sufficient evidence has been demonstrated to conclude without further questions or risk assessment.

The FSA/FSS conclude that the *Lactiplantibacillus plantarum* NCIMB 30084 silage additive, as described in this application, is safe and is not liable to have an adverse effect on the target species, environmental safety and human health at the intended concentrations of use. In the absence of data for assessment, the additive should be regarded as a potential skin and eye irritant, and due to the proteinaceous nature of the product, it is considered to be a respiratory sensitiser.

In making this assessment, the following principles have been applied:

1) There is not a legal duty to perform a separate risk assessment for GB and therefore, there was sufficient scientific evidence to make a conclusion on safety with no further questions to the applicant, and therefore no further risk assessment activities are necessary.

2) The application is for a renewal or authorisation where the UK/GB already has accepted the established risk of the products on the market.

3) Sufficient evidence was available in the literature, for example, where other National food safety authorities had positively assessed the application using the same risk assessment guidance in principle and legal requirements in GB with the exception to changes in the General Food Law.

4) Applicants provided sufficient relevant information as requested by FSA/FSS.

5) The FSA/FSS review did not find any issues of divergence from guidance or mutual approaches or new scientific issues for consideration.

6) There were no other specific issues that would require an assessment for the UK or the nations of the UK.

8. References

1. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2023. Assessment of the feed additive consisting of Lactiplantibacillus plantarum (formerly Lactobacillus plantarum) NCIMB 30084 for all animal species for the renewal of its authorisation (Chr. Hansen A/S). EFSA Journal 2023; 21(7):8167. 8 pp. https://doi.org/10.2903/j.efsa.2023.8167

2. EC (European Commission), 2003. Regulation No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition. Available at Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition (Text with EEA relevance) (legislation.gov.uk)

3. EC (European Commission), 2013. Regulation No 308/2013 concerning the authorisation of a preparation of Lactobacillus plantarum NCIMB 30083 and of a preparation of Lactobacillus plantarum NCIMB 30084 as feed additives for all animal species. Available at Implementing regulation - 308/2013 - EN - EUR-Lex (europa.eu)

4. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2021. Guidance on the renewal of the authorisation of feed additives. EFSA journal 2021;19(1):6340, 14 pp. https://doi.org/10.2903/j.efsa.2021.6340

5. EC (European Commission), 2008. Regulation No 429/2008 of the European Parliament and of the Council on additives for use in animal nutrition. Available at Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications

and the assessment and the authorisation of feed additives (Text with EEA relevance) (legislation.gov.uk)

6. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2013. Scientific Opinion on the safety and efficacy of Lactobacillus plantarum (NCIMB 30083 and NCIMB 30084) as a feed additive for all species. EFSA Journal 2013; 11(1):3041. https://doi.org/10.2903/j.efsa.2013.3041

7. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018. Guidance on the characterisation of microorganisms used as feed additives or as production organisms. *EFSA Journal* 2018;16(3):5206, 24 pp. https://doi.org/10.2903/j.efsa.2018.5206

8. EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2023. Scientific Opinion on the update of the list of qualified presumption of safety (QPS) recommended microorganisms intentionally added to food or feed as notified to EFSA. EFSA Journal 2023;21(1):7747, 23 pp https://doi.org/10.2903/j.efsa.2023.7747

9. EURL-FA (European Reference Laboratory for Feed Additives), 2012. EURL Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003. Fifteen “micro-organisms used as silage agents”. Available at Final Report FAD-2010-0135 FAD-2010-0302 - FAD-2010-0387 - FAD-2010-0388 - FAD-2010-0389 - FAD-2010-0395 (europa.eu)

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